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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,770	12/17/2001	Yoshihito Ikeda	F-7178	2012

277 7590 03/29/2005

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EXAMINER

PRATS, FRANCISCO CHANDLER

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 03/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.		Applicant(s)	
	10/018,770		IKEDA ET AL.	
	Examiner		Art Unit	
	Francisco C. Prats		1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 December 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 4, 6-8, 10-14 and 19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 4, 6-8, 10-14 and 19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- 1. ☐ Certified copies of the priority documents have been received.
 - 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
6) <input type="checkbox"/> Other: _____ |
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DETAILED ACTION

The amendment filed December 23, 2004, has been received and entered. The Rule 132 Declaration of Dr. Yoshitomi Morizawa, filed December 23, 2004, has been received and considered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 1, 4, 6-8, 10-14 and 19 are pending and are examined on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35

U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4, 6-8, 10-14 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 9-117279 in view of JP 1-304882.

JP '279 discloses the preparation of the claimed lecithin-derived SOD for therapeutic uses. See English language abstract; see also page 4 of English translation. JP '279 differs from the cited claims in not combining the SOD derivative with a carrier which allows for the storage properties recited in the claims. However, JP '882 clearly discloses that combination of SOD with sucrose results in a stable SOD preparation suitable for storage. See English language abstract; see also "Embodiment 3", at pages 9 and 10 of the English translation.

Thus, the artisan of ordinary skill seeking to store the SOD derivatives of JP '279, recognizing from JP '882 that addition of sucrose would improve the storage stability of the SOD derivatives, clearly would have been motivated by JP '882 to have combined the SOD derivatives of '279 with sucrose to have rendered them stable for storage. A reasonable expectation of success would have been based on the fact that JP '882 discloses that the very same enzyme was rendered storage stable by

combination with sucrose. A holding of obviousness is therefore required.

All of applicant's argument submitted to date regarding this ground of rejection has again been fully considered, and reconsidered, but is not persuasive of error. It is noted, as argued by applicant, and ably demonstrated by the experiment presented in the Rule 132 Declaration of Dr. Morizawa, that the degradation of PC-SOD during storage at varying temperatures results in a pH increase accompanied by an apparent cleavage event which results in the release of palmitic acid into the storage medium. However, with all due respect, the presented evidence does not demonstrate non-obviousness.

One of ordinary skill clearly would have recognized that degradation of PC-SOD and SOD would have yielded at least some different degradation products, in view of the art-recognized fact that PC-SOD has a pendant phosphatidylcholine group attached to the enzyme protein, whereas SOD does not have the pendant phosphatidylcholine group. However, one critical fact absent from applicant's analysis is the fact that the portion of the PC-SOD compound which actually catalyzes chemical reactions is identical to the catalytic portion of the underivatized SOD compound. That is, the catalytic portions of the two compounds, PC-SOD and SOD, are identical. Thus, one of ordinary skill

looking to preserve catalytic activity of PC-SOD clearly would have first looked to compounds which were known to preserve the catalytic activity of SOD, such as the sucrose recited in the claims under examination.

Applicant urges that PC-SOD and SOD lose their activities by different mechanisms. However, applicant fails to provide any factual support for this assertion. Reference to page 16 of the specification makes it clear that applicant considers the drug utility of PC-SOD to be lost upon cleavage of the phosphatidylcholine. This is much different than saying that catalytic activity of the enzyme is lost. The fact is that enzymes, which are proteins, lose catalytic activity for a number of reasons, including the loss of the three-dimensional structure which allows the catalyzed reaction to occur (i.e. denaturation of the protein resulting in destruction of the active site), or steric hindrance (i.e. blocking of the active site). Thus, while applicant urges that neither preservation of the active site nor the common utility of PC-SOD and SOD are relevant to the degradation of the compounds, this is simply incorrect from a scientific standpoint. One of ordinary skill seeking compounds to preserve PC-SOD clearly would have looked to compounds known to have preserved catalytic activity of SOD.

Moreover, with respect to the preservation of the actual catalytic activity critical to the utility of the compounds, the experiments presented by applicant do not assess the actual activity of the two compounds. Rather, the experiments presented by applicant demonstrate that degradation of PC-SOD includes the release of certain moieties which would not have been expected to have been released upon degradation of underivatized SOD. Contrary to applicant's argument, the presented experiments demonstrate nothing about the mechanism of loss of *catalytic activity* of PC-SOD vis-à-vis SOD, especially since no assay of enzyme activity was performed. Thus, while applicant asserts that "PC-SOD and SOD degrade by entirely different mechanisms" (response, page 6), applicant has failed to demonstrate that the "entirely different mechanisms" are in any way related to the *catalytic activity* of the two molecules. Moreover, from a scientific standpoint, the argument that "PC-SOD and SOD degrade by entirely different mechanisms, neither of which is related to its utility or active site" (response, page 6), is simply incorrect with respect to the catalytic activity of the compounds. The catalytic activity of a therapeutic enzyme, and hence the enzyme's utility, is inextricably linked to the enzyme's active site. If catalytic activity is lost, the degradation is necessarily somehow related to the active site.

Further still, the fact that known SOD preservatives other than sucrose (alanine, inositol, mannitol, etc.) do not function in the same manner as sucrose does not demonstrate non-obviousness. A holding of *prima facie* obviousness does not require absolute predictability. In the instant case applicant has applied a known SOD preservative in the preservation of PC-SOD. Thus, the same preservative has been applied to a compound having the same utility and almost an identical structure, as that in the prior art.

Again, motivation for using sucrose as a PC-SOD preservative would have been derived from the recognition that PC-SOD and SOD share an identical chemical structure with respect to that portion of the molecule responsible for catalyzing chemical reactions. As argued by applicant, and demonstrated by the Rule 132 Declaration presented herein, one of ordinary skill may have expected certain of the degradation products of PC-SOD and SOD to have been different. However, because the catalytic portions of the PC-SOD and SOD molecules are identical, the recognition of non-identical degradation products would not have led the artisan of ordinary skill seeking to stabilize PC-SOD away from compounds known to preserve the identical catalytic activity of SOD under storage conditions. Rather, because the catalytic portions of the two

compounds are identical, the artisan of ordinary skill would have reasonably expected compounds which preserve SOD catalytic activity to have also preserved PC-SOD catalytic activity, and would therefore have been motivated to have used SOD-preservative compounds, including the claimed sucrose, to have preserved PC-SOD, as recited in the pending claims.

No claims are allowed.

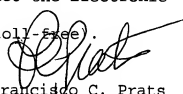
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C. Prats whose telephone number is 571-272-0921. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Francisco C. Prats
Primary Examiner
Art Unit 1651